

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/03583

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :A61K 38/00; C07K 1/00; C07H 21/04; C12P 21/06; G01N 33/566  
US CL :514/2; 530/350, 388.22; 536/23.5; 435/69.1; 436/501

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/2; 530/350, 388.22; 536/23.5; 435/69.1; 436/501

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Please See Extra Sheet.

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	SPARATORE et al. Extracellular high-mobility group 1 protein is essential for murine erythroleukemia cell differentiation. Biochem. J. August 1996, Vol. 320, pages 253-256, see the Abstract.	1-3
A	WANG, H. et al. HMG-1 as a late mediator of endotoxin lethality in mice. Science. 09 July 1999, Vol. 285, pages 248-251, see the entire document.	1-8

Further documents are listed in the continuation of Box C.

See patent family annex.

*A*	Special categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance	*T*	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
*E*	earlier document published on or after the international filing date	*X*	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
*L*	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	*Y*	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
*O*	document referring to an oral disclosure, use, exhibition or other means	*&*	document member of the same patent family
*P*	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

28 MARCH 2001

Date of mailing of the international search report

23 MAY 2001

Name and mailing address of the ISA/US  
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**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-8

**Remark on Protest**  

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

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**B. FIELDS SEARCHED**

Electronic data bases consulted (Name of data base and where practicable terms used):

**STN: MEDLINE, BIOSIS, BIOTECHNO; WEST 2.0**

search terms: HMG1 antagonist, anti-HMG1, antibody, sepsis, inflammatory cascade, high mobility group, amphotericin, anti-amphotericin

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING**

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-8, drawn to a pharmaceutical composition for treating disease comprising an antagonist of HMG1 and a method for treating disease characterized by activation of the inflammatory cytokine cascade.

Group II, claim(s) 9-11, drawn to a diagnostic method.

Group III, claim(s) 12, drawn to a pharmaceutical composition for effecting weight loss.

Group IV, claim 13, drawn to a method for effecting weight loss.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack Unity of Invention because they are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for more than one species to be searched, the appropriate additional search fees must be paid. The species are as follows:

A pharmaceutical composition comprising:

- i) an antibody,
- ii) an antisense nucleic acid,
- iii) and HMG1 receptor antagonist

The claims are deemed to correspond to the species listed above in the following manner:

Claims 1-8 require the above species of compounds

The following claims are generic: 1-8

The inventions listed as Groups do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Pursuant to 37 C.F.R. 1.475(d), this Authority considers that the main invention in the instant application comprises the first recited product, a pharmaceutical composition comprising an HMG1 receptor antagonist and the first recited method of using that product, namely in the process of treating a condition characterized by activation of the inflammatory cytokine cascade. Further, pursuant to 37 C.F.R. 1.475(b)-(d), the ISA/US considers that the materially and functionally dissimilar products of Groups III and the additional methods of Groups II and IV do not correspond to the main invention. This Authority therefore considers that the several inventions do not share a special technical feature within the meaning of PCT Rule 13.2 and thus do not relate to a single general inventive concept within the meaning of PCT Rule 13.1.

The species listed above do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Antibodies, nucleic acids and molecules which function as HMG1 receptor antagonists are functionally and structurally distinct compounds.